Title: Biologics for psoriasis in COVID-19 era: what do we know?

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Dear Editor,

we have read with great interest the article by Conforti et al. who stressed the importance of a therapeutic reassessment of all psoriatic patients, chronically treated with immunosuppressive drugs in the pandemic coronavirus disease (COVID)-19 era.[1] In the context of Dermatology, psoriasis patients represent an important subset since their prevalence (125 million worldwide). Literature, mass media and information campaigns are daily focusing on preventive measures, risk factors and class of subjects which are at increased risk, in order to sensitize the general population, and limit behaviors which could facilitate virus diffusion. We agree that whether stopping or not these treatments in psoriasis patients represents a hot and unsolved topic which needs to be further investigated. However, definitive evidences that anti-psoriatic biologics increase the risk of infectious complications and promote the spreading of COVID-19 are lacking. Indeed, both the Italian Society of Dermatology and the International Psoriasis council recommend to stop biologic treatment only in case of documented COVID-19 and/or active symptoms such as fever, cough and shortness of breath. The immune responses against COVID-19 leads to T cell activation and differentiation, including the production of cytokines associated with the different T cell subsets (ie, Th17), followed by a massive release of cytokines in infected cells in response to coronavirus-19 infection.[2,3] The release of this big amount of cytokines may be responsible for a cytokine storm which further damage organs (mainly lungs) aggravating the clinical course of the infected patients. Indeed, COVID-19 subjects, particularly those requiring intensive care, showed increased levels of IL-17 and TNF-α[3] which are well known targets of biologics used for psoriasis treatment. Moreover, Chinese National Health Commission issued guidelines recommending tocilizumab, a biologic drug used for rheumatoid arthritis which blocks IL-6 action, for COVID-19 severe complications. Hence, the question whether other biologics blocking IL-17 or TNF-α may be even ameliorate the immune response towards COVID-19, avoiding the cytokine storm which can lead to severe lung damage, is raising. As regards IL-17, Xu et al. observed that T cells overactivation,

manifested by increase of Th17 and high cytotoxicity of CD8 T cells, accounted for a severe immune injury in their COVID-19 case report, also highlighting that the pathological features of COVID-19 greatly resemble those seen in Severe Acute Respiratory Syndrome (SARS) and Middle Eastern respiratory syndrome (MERS) coronavirus infection.[4] Indeed, it has been reported that IL-17 commonly produced during SARS specifically augments a pro-inflammatory response by directly synergizing with antiviral signaling, thus exerting excessive inflammation which is destructive for the lungs.[5] Moreover, examining all possible therapeutic targets for COVID-19 in their recent article on Lancet, Zumla et al. also hypothesize that blocking IL-17 could have the potential to improve COVID-19's aberrant immune response and acute respiratory distress syndrome-related mortality.[6] Indeed, a Chinese clinical trial evaluating an anti-IL17 drug approved for psoriasis and psoriatic arthritis, ixekizumab, is already running.[7] Therefore, since definitive evidences that biologics blocking TNF-α and anti-IL17 increase the risk of COVID-19 is lacking, we believe that preventive treatment discontinuation should be avoided and reserved to COVID-19 patients, subjects with active symptoms or who have had a contact to a confirmed COVID-19 patient. Indeed, unnecessary biologic discontinuation would lead to a worsening of psoriasis and psoriatic arthritis in a high percentage of the cases. As a consequence, there may be higher disease burden, destructive impact on quality of life, as well as increased health care costs due to the augmented number of consultations and recovery. Furthermore, the unavoidable subsequent return to biologic therapy could be associated with switching toward higher cost drugs, due to the well-known lower efficacy of biologics in the same patient after their interruption.[8]

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